DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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WARNING LETTER

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

VIA FEDERAL EXPRESS

JUL 26 2004

Hans C. Kioschos, M.D.
[redacted]
508 Stocktrail Ave., Suite A.
Gillette, WY 82716

Dear Dr. Kioschos:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site and to request that prompt corrective actions be taken. Mr. Blake Jansen, an investigator from the FDA's Denver District Office, conducted the inspection during the period of April 5 through 8, 2004. The purpose of the inspection was to determine whether your activities as a clinical investigator (CI) of an investigational study [redacted] complied with applicable FDA regulations. The [redacted] is a device as defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C 321(h)].

The FDA conducted the inspection under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), and Premarket Notification [510(k)] submissions are scientifically valid and accurate. The program also ensures that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 812- Investigational Device Exemptions and Section 520(g) of the Act [21 U.S.C. 360j(g)]. At the close of the inspection, Mr. Blake Jansen presented a Form FDA 483 "Inspectional Observations" to you for review and discussed the listed deviations. The deviations noted on the Form FDA 483 and our subsequent inspection report review are discussed below:

Failure to ensure that the investigation is conducted according to the investigational plan and FDA regulations [21 CFR 812.100 and 812.110 (b)]; Failure to obtain IRB approval of the investigation [21 CFR 812.110(a)].

Pursuant to 21 CFR 812.100 and 812.110 (b), an investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan, which includes the study protocol, applicable FDA regulations, and any conditions

of approval imposed by an IRB or FDA. Under 21 CFR 812.110(a), an investigator may not solicit written informed consent or permit a subject to participate in an investigation before obtaining IRB approval. You failed to fulfill these obligations. For example:

- You conducted the investigation using study protocol version "Rev 00," which had yet to be reviewed or approved by your IRB. On January 1, 2003, the IRB approved the study protocol dated May 7, 2001, and indicated in their approval letter that you must obtain pre-approval for changes in research activity. Under 21 CFR 812.110(a), IRB approval is also required prior to implementation of any changed investigational plan or protocol.

- You made numerous deviations from the protocol. For example:

  - You failed to exclude subjects who did not meet the inclusion criteria. [redacted] of the [redacted] subjects failed one or more of the following criteria: they required [redacted] exceeded the maximum allowable [redacted] had no documentation affirming [redacted] and/or indicated that they would not be available for post-operative follow-up visits. Furthermore, you failed to assess the [redacted] for [redacted] of the [redacted] subjects enrolled, which is required for inclusion into the study.

  - You failed to measure the subjects' Body Mass Index (BMI) in accordance to the standard defined by Association for the Study of Obesity as required by the study protocol. Furthermore, you failed to document the alternative method used by you for calculating the BMI or the actual BMI for the subjects.

  - You failed to perform required follow-up visits in a timely manner, as specified in the protocol. At least [redacted] of the [redacted] follow-up visits for [redacted] subject were not conducted in accordance with the time frames set forth by the protocol.

Failure to maintain accurate, complete and current records [21 CFR 812.140(a)]

Investigators must maintain accurate, complete, and current records related to the receipt, use, or disposition of a device, as well as accurate, complete and current records of each subject's case history and exposure to the device, including case report forms (CRFs). 21 CFR 812.140(a)(2) & (3) . You failed to fulfill these requirements. For example:

- There were discrepancies in the study documents regarding which lot number of the device was actually implanted in the study subjects for all [redacted] subjects who had received the device. For example:

    - The form titled Kit Router states the [redacted], Lot [redacted] was "missing." A second [redacted], Lot [redacted], was received, however, the documents titled Implant Usage Ticket and Operative state that Lot [redacted] was implanted in Subject [redacted].

    - The form titled Kit Router states the [redacted], Lot # [redacted] was returned and was missing. This form also states a replacement [redacted], Lot # [redacted], was received. The Patient Tracking Log states the [redacted] Lot # [redacted] was implanted in Subject [redacted]

    - The form titled Kit Router states [redacted] Lot [redacted] was "missing". A second [redacted], Lot # [redacted] was received, however, the document titled Operative stated that Lot # [redacted] was implanted in Subject [redacted].

    - The Patient Tracking Log states that Subject [redacted] received a [redacted] Insert, Lot # [redacted]. However, the CRF #3 titled Operative states that a [redacted] Lot # [redacted], was implanted in this subject.

    - The form titled Kit Router states that [redacted], Lot # [redacted] was lost and a replacement unit, Lot # [redacted] was received, however, the document titled Operative states [redacted] Lot # [redacted] was implanted in Subject [redacted]

- Of the [redacted] study subjects, you failed to complete the case report forms for [redacted] subjects' three-month visits; [redacted] subjects' six-month visits and [redacted] subject's twelve-month visit, although records document that such visits had occurred.

- The source documents for [redacted] for [redacted] subject conflicted with the case report form.

The above-described violations are not intended to be an all-inclusive list of deficiencies that may exist in this clinical study. It is your responsibility as a clinical investigator to assure adherence to each requirement of the Act and all applicable federal regulations. For further information related to clinical investigators' obligations, please visit our web site at http://www.fda.gov/oc/ohrt/irbs/default.htm.

Within 15 working days after receiving this letter please provide written documentation of the specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current and future studies. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings in accordance with 21 CFR 812.119.

Send your response to: Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
Program Enforcement Branch II (HFZ-312)
2094 Gaither Road
Rockville, MD 20850
Attn: Linda Godfrey

We are also sending a copy of this letter to FDA's Chicago District Office and request that you also send a copy of your response to that office. If you have any questions, please contact Linda Godfrey, Consumer Safety Officer at 301-594-4723 ext. 134 or by email at Linda.Godfrey@fda.hhs.gov.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

cc:

[redacted]
General Manager
[redacted]

(purged)